UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,246	04/02/2001	Sharat Singh	0225-0033.20	4459

33603 7590 05/21/2003

ACLARA BIOSCIENCES, INC.
1288 PEAR AVENUE
MOUNTAIN VIEW, CA 94043

EXAMINER
TUNG, JOYCE

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/825,246	Singh et al.
Examiner	**Art Unit**
Joyce Tung	1637

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 21, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *16, 17, and 19-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *16, 17, and 19-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: notice to comply with Sequence rules

DETAILED ACTION

Response to Amendment

1. The applicant's Response filed 2/21/2003 has been entered-in-part. The part of the amendment showing the sequence listing has not been entered. It should start on a separate piece of paper and should be identical to the CRF provided.

Following the entry of the applicant's amendment, claims 16-17 and 19-29 are pending.

2. The rejection of claims 18 and 20 under 35 U.S.C. 112 second paragraph is withdrawn.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 16-17. 19-21 and 23-24 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman (5,470,705(1995)) in view of Babon et al. (5,851,770 (1998)).

Grossman et al. disclose a method of detecting a plurality of different sequences in a target sequence involving a plurality of sequence probes (See column 2, lines 54-56). The probe comprises the features of the e-tag probe claimed in claims 16-17, 19-21 and 23-24. The probe includes a binding polymer, a polymer chain which imparts to that probe, a distinctive ratio of charge/translational frictional drag and a reporter attached to the binding polymer (See column 20, lines 52-57). The binding polymer is an oligonucleotide including at least 10-20 bases allowing hybridization to the target polynucleotide (See column 6, lines 66-67 and column 7, lines 1-10). Other binding polymers are analogs of polynucleotides, such as deoxynucleotides with thiophosphodiester linkage (See column 7, lines 11-19). The polymer chain has a ratio of charge/translational frictional drag which is evidenced by a distinctive electrophoretic mobility in a non-sieving matrix (See column 7, lines 50-64). The polymer chain can be polyethylene oxide (PEO) or a polypeptide chain where the chains are attached to different-sequence binding polymers (See column 3, lines 11-18). The teachings suggest that the charge/translational frictional drag is consisted of carbon, hydrogen, oxygen, phosphorus, nitrogen, sulfur and boron

recited in claim 24. The label refers to a fluorophore or chromophore (See column 6, lines 39-44). The features of Grossman et al.'s probe suggest the features of the claimed e-tag probe.

Grossman et al do no disclose the probe attached to a capture ligand.

Babon et al. disclose a method for detecting one or more mismatches between a first and second nucleic acid in which the heteroduplex formed between the first and second nucleic acid sequence is biotinylated and captured by binding to streptavidin-magnetic beads (See column 7, lines 53-66). The capture ligand and capture agent include antigen/antibody or DNA binding protein and its DNA binding site (See column 18, lines 13-24).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to modify the probe of Grossman et al. wherein the capture ligand and agent are attached to the oligonucleotide probe as taught by Babon et al.. The ordinary artisan would have been motivated to make this invention because directly capturing the probe to a solid support is easy to wash away the unbound probe which increases the accuracy of the method instead of capturing the probe through the immobilized target sequence as disclosed by Grossman et al.

The response argues that Grossman et al. do not disclose capture moieties attached to probes and non oligomeric compound to generate distinct electrophoretic mobilities.

Grossman et al. disclose that the polymer chain has a ratio of charge/translational frictional drag (See column 7, lines 49-52). The distinctive ratio of charge/translational frictional drag is typically achieved by difference in lengths of the polymer chain (See column 7, lines 59-

62). The polymer chain are formed by polyethylene oxide or polyglycolic acid (See column 7, lines 43-49).

The newly added phrase "non-oligomeric compound" which is consisting of from 1 to 500 atoms. The phrase "non-oligomeric compound" is defined in the specification that non-oligomeric compound is a compound which is not oligonucleotide or polypeptide (See pg. 30, lines 24-31 of the specification). As indicated above, the polymer chain in the probe of Grossman et al. is read on the limitation of "non-oligomeric compound" because the polymer chain are formed by polyethylene oxide or polyglycolic acid or polypeptide (See column 7, lines 43-49).

Babon et al. disclose a method for detecting one or more mismatches between a first and second nucleic acid in which the heteroduplex formed between the first and second nucleic acid sequence is biotinylated and captured by binding to streptavidin-magnetic beads (See column 7, lines 53-66).

The response further argues that the capture ligands of Applicants' are not used in a wash step. However, the claim language indicates that the capture ligand specifically binds to a capture agent to exclude undigested electrophoretic probe from the electropherogram (See claims 16 and 25). Therefore, the uses of capture ligand in the instant invention and in the teachings of Babon et al. are for separation. In addition, the function language does not have the patentable weight. Thus, the rejection is maintained.

4. Claim 22 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705 (1995)) in view of Babon et al. (5,851,770 (1998)) as applied to claims 16-17, 19-21 and 23-24 above, and further in view of Huie et al. (5,470,967 (1995)).

The teachings of Grossman et al. and Babon et al. are set forth in section 3 above. none of the references discloses that said oligonucleotide has at least one nuclease resistant linkage.

Huie et al. disclose phosphodiester linkage in oligonucleotide analogs (See column 3, lines 59-62) and phosphorothioate diester shows increased resistance to nuclease (See column 3, lines 59-67).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to use phosphodiester linkage as indicated by Huie et al. in the oligonucleotide probe of Grossman et al. to resist nuclease activity because the use of modified linkage within the oligonucleotide makes them nuclease resistant (See column 3, lines 63-67).

The response argues that Huie et al. is concerned with the use of nuclease resistant oligonucleotide for therapeutic purpose, while the instant invention is to use nuclease resistant oligonucleotide for the cleavage of the probe at the same internucleoside linkage. However, the claim language does not limit to that the nuclease-resistant linkage is at the same internucleoside of the probe. Thus, the rejection is maintained.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 25-28 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705 (1995)) in view of Babon et al. (5,851,770 (1998)).

The teachings of Grossman et al. and Babon et al. are set forth in section 3 above. Since the limitations of claims 25-28 are similar with the limitations of claims 16-17 19-21 and 23-24, as discussed in section 3 above, the teachings of Grossman et al. and Babon et al. are also applied to the limitations of claims 25-28.

7. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705 (1995)) in view of Babon et al. (5,851,770 (1998)) as applied to claims 25-28 above, and further in view of Ullman et al. (6,251,581B1 (2001))

Grossman et al. and Babon et al. do not disclose the detectable labels which are the compounds listed in claim 29.

Ullman et al. disclose a method for determining an analyte in a medium (See the Abstract). The method applies a chemiluminescent compound associated with an specific binding pair member (See column 4, lines 54-65 and column 5, lines 8-14). The compound has the same structure as the compound listed in claims 29 (See column 42-58).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply the chemiluminescent compound of Ullman et al. to the probe of Grossman et al. in order to construct a set of electrophoretic tag probe of instant invention. The substitution of one known reagent with known properties for a second well known reagent with known properties would have been prima facie obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. Thus it would have been prima facie obvious to apply the fluorescent molecules to the electrophoric release tag to construct the set of electrophoretic tag probe.

SEQUENCE RULES

8. This application still fails to comply with the requirement of 37 CFR 1.821 through 1.825. Note that the CRF is technically flawed and cannot be entered into the database. See also

the Notice to comply With Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

SUMMARY

9. No claims are allowable.

CONCLUSION

10. Claims 16-17 and 19-29 are rejected and/or objected to for the reasons set forth above.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

J.T

May 12, 2003

Ethan Whisenant, Ph.D.
Primary Examiner
Art Unit 1634